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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,541	03/07/2001	Liselotte Bjerre Knudsen	6169.200-US	4130

7590 12/02/2003

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,541	KNUDSEN, LISELOTTE BJERRE	
	Examiner	Art Unit	
	David S Romeo	1647	

-- Th MAILING DATE of this communication appears on the cover she t with th c rrespondenc ddress --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29 and 36-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29 and 36-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *26-29 and 36-72* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed August 25, 2003 has been entered. Claims 26-29, 36-72 are pending. Applicant's election of group I, claims 26-29, 36-42, and the species Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 26-29, 36-72 are being examined to the extent that they read upon the species Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37).

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 102

Claims 26-29, 36-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Eng (a11) in view of Raufman (u11) and in view of Howard (v11).

The rejection of record is applied to claims 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, 72. Exendin-3 or exendin-4 are an analog or derivative or a derivative of an analogue of GLP-1(7-37) or exendin-4, as recited in claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72, in the absence of evidence to the contrary. In the presence of evidence to the contrary claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant argues that the examiner would have to demonstrate that every diabetic patient mentioned in Eng would necessarily be a patient in need of having their serum lipids lowered. Applicant's arguments have been fully considered but they are not persuasive. Eng discloses pharmaceutical compositions containing exendin-3 or exendin-

4, or any combination thereof, and methods for the treatment of diabetes mellitus and the prevention of hyperglycemia (column 2, lines 35-40). Hence, Eng discloses the treatment of diabetes mellitus in any and/or all such diabetic patients. The cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (Howard, page 219, left column). Hence, any and/or all such diabetic patients clearly encompasses diabetic patients with dyslipidemia, hyperglycemia, hypertension, and/or obesity. Alternatively, the treatment of dyslipidemia, as claimed, clearly overlaps the treatment of diabetes and/or obesity. In addition, Howard (v11), Kreisberg (cited by Applicant), and Wilson (cited by Applicant) are all evidence that "patient in need of such treatment" (the missing descriptive matter) is necessarily present in Eng's treatment of diabetes mellitus (the thing described in the reference), and that it would be so recognized by persons of ordinary skill. Furthermore, it is not necessary that that "patient in need of such treatment" (the missing descriptive matter) necessarily be present in Eng's treatment of diabetes mellitus (the thing described in the reference), and that it would be so recognized by persons of ordinary skill, because any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment. Hence, it is not necessary that the examiner demonstrate that every diabetic patient mentioned in Eng would necessarily be a patient in need of having their serum lipids lowered.

Applicant's traverse of examiner using the present specification as a definition of the term "patient in need of such treatment" is noted. However, the examiner is merely saying that the examiner's interpretation of the limitation "patient in need of such treatment" is commensurate with the present specification at page 2, full paragraph 2.

Specifically, any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2.

Claims 26, 27, 29, 36, 37, 39, 40, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Efendic (b11) in view of Howard (v11).

The rejection of record is applied to claims 43-46, 48, 49, 52-56, 58, 59, 62-66, 68, 69, 72. GLP-1 (7-36)amide is an analog or derivative or a derivative of an analogue of GLP-1(7-37) or exendin-4, as recited in claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72, in the absence of evidence to the contrary. In the presence of evidence to the contrary claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant argues that a rejection based on inherent anticipation over Efendic would require that every obese patient with NIDDM be a patient in need of having their serum lipids lowered. Applicant's arguments have been fully considered but they are not persuasive.

Efendic discloses infusing GLP-1 (7-36)amide at a rate of 0.75 pmol per kilogram of body weight per minute in insulin treated obese NIDDM patients (paragraph bridging columns 5-6). Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in

accordance with the present specification at page 2, full paragraph 2. It is not necessary that a "patient in need of such treatment" (the missing descriptive matter) necessarily be present in Efendic's treatment (the thing described in the reference), and that it would be so recognized by persons of ordinary skill, because any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment. Hence, it is not necessary that the examiner demonstrate that every obese/diabetic patient would necessarily be a patient in need of having their serum lipids lowered.

Applicant's traverse of examiner using the present specification as a definition of the term "patient in need of such treatment" is noted. However, the examiner is merely saying that the examiner's interpretation of the limitation "patient in need of such treatment" is commensurate with the present specification at page 2, full paragraph 2. Specifically, any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2.

Claim Rejections - 35 USC § 112

Claims 26-29, 36-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering plasma levels of triglycerides, free fatty acids, or total cholesterol, does not reasonably provide enablement for a method of lowering one or more serum lipids, of reducing the serum LDL:HDL ratio, or of reducing the serum level of lp(A) or apo(A).

The rejection of record is applied to claims 43-72.

Applicant argues that the absence of working examples does not mean that the claims are not enabled. Applicant's arguments have been fully considered but they are not persuasive. Lack of a working example is a factor to be considered, and the present rejection does not rely solely on the lack of a working example.

Applicant argues that Juntti-Berggren does not provide any evidence to doubt the objective truth of the present disclosure because insulin exerts its own effects on lipid levels. Applicant's arguments have been fully considered but they are not persuasive because Applicant's argument and the Howard article (cited by Applicants) do not explain the lack of effect of GLP-1 on the levels of LDL and HDL.

Claims 26-29, 36-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of record is applied to claims 43-72.

Applicant argues that the presence of working examples is not required. Applicant's arguments have been fully considered but they are not persuasive. The examiner did not require the presence of a working example. The examiner stated that no specific guidance for, or working examples of, practicing the invention commensurate with the full scope of the claims is described. Furthermore, the written description provision of 35 USC 112 is severable from its enablement provision.

Applicant argues that Juntti-Berggren does not provide any evidence to doubt the objective truth of the present disclosure because insulin exerts its own effects on lipid levels. Applicant's arguments have been fully considered but they are not persuasive because Applicant's argument and the Howard article (cited by Applicants) do not explain the lack of effect of GLP-1 on the levels of LDL and HDL.

Claims 26, 27, 29, 36, 37, 39, 40, 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of record is applied to claims 44-49, 52, 54-59, 62, 64-69, 72.

Applicant argues that the rejection is rendered moot by amending the claims to recite "GLP-1 agonist is ... or an analogue of derivative of any of the foregoing." Applicant's arguments have been fully considered but they are not persuasive. The term "analogue" or "derivative," "derivative of an analogue," or "exendin-4 analogue" is a genus of compounds. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any structural limitations on the structure of the agonist. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because there are no structural limitations to the genus. See, for example, the GLP-1 agonists compounds of Banchovin (1, cited by Applicants). Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general

knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Although it might be obvious for the skilled artisan to screen for compounds with GLP-1 agonist activity, the written description requirement is not satisfied by that which is obvious over what is disclosed; it is satisfied by that which is disclosed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the specific structural analogs of GLP-1 disclosed in the preset specification, alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Double Patenting

Claims 26-29, 36-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39, 40 of U.S. Patent No. 6,268,343 (c11) in view of Howard (v11) and Efendic (b11).

The rejection of record is applied to claims 44-50, 52, 54-60, 62, 64-70, 72. Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) is an analog or derivative or a derivative of an analogue of GLP-1(7-37) or exendin-4, as recited in claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72, in the absence of evidence to the contrary. In the presence of evidence to the contrary claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 26-29, 36-42 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 of copending Application No. 6,458,924 (d11) in view of Howard (v11) and Efendic (b11).

The rejection of record is applied to claims 44-50, 52, 54-60, 62, 64-70, 72. Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) is an analog or derivative or a derivative of an analogue of GLP-1(7-37) or exendin-4, as recited in claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72, in the absence of evidence to the contrary. In the presence of evidence to the contrary claims 44-46, 48, 49, 52, 54-56, 58, 59, 62, 64-66, 68, 69, 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant's traverse of examiner using the present specification as a definition of the term "patient in need of such treatment" is noted. However, the examiner is merely saying that the examiner's interpretation of the limitation "patient in need of such treatment" is commensurate with the present specification at page 2, full paragraph 2. Specifically, any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2.

Applicant argues that Applicant has provided evidence that not all diabetic and/or obese patients are patients with elevated serum lipids. Applicant's arguments have been fully considered but they are not persuasive.

The treatment of obesity or diabetes, as claimed in the patents, clearly overlaps the treatment of dyslipidemia, as presently claimed, as evidenced by Howard and Efendic. Howard (v11), Efendic (b11), Kreisberg (cited by Applicant), and Wilson (cited by Applicant) are all evidence that "patient in need of such treatment" (the missing descriptive matter), as presently claimed, is necessarily present in the patents' treatment of diabetes or obesity (the thing described in the reference), and that it would be so recognized by persons of ordinary skill. Hence, it is not necessary that the examiner demonstrate that every diabetic or obese patient in the claims of the patents is necessarily a patient in need of having their serum lipids lowered.

New Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 44-49, 52, 54-59, 62, 64-69, 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 44-49, 52, 54-59, 62, 64-69, 72 are indefinite because they recite the term "analogue" or "derivative," "derivative of an analogue," or "exendin-4 analogue." Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "analogue" or "derivative," "derivative of an analogue," or "exendin-4 analogue" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 45, 49, 55, 59, 65, 69 are indefinite because it is unclear if the analog is GLP-1(7-37) with a single amino acid substitution or some wholly undefined compound comprising an amino acid that is different from an amino acid in the corresponding position of GLP-1(7-37). The metes and bounds are not clearly set forth.

Conclusion

No claims are allowable. Claims limited to a method of lowering plasma levels of triglycerides, free fatty acids, or total cholesterol comprising administering Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) would be allowable upon the filing of appropriate terminal disclaimers.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

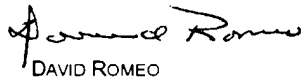
BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
NOVEMBER 29, 2003